

REGION SPECIFIC EFFECTS OF ANTIPSYCHOTIC DRUGS ON RAT
STRIATAL NEUROTENSIN (NT) GENE EXPRESSION.

Kalpana M. Merchant, Dorcas J. Dobie, and Daniel M. Dorsa, Depts. of Psychiatry and Behavioral Sciences and Pharmacology, University of Washington, Seattle, WA 98195.

We have recently reported that acute administration of haloperidol dramatically increases expression of NT mRNA in the dorsolateral striatum (DLST) and shell region of the nucleus accumbens (sNA). The DLST effect appears to be due to an increase in transcription of the NT gene. We have compared these effects to those of other typical neuroleptics such as fluphenazine, and to the newer "atypical" agents which have a lower propensity to induce motor side effects such as clozapine, thioridazine, and remoxipride. In situ hybridization methods were used to quantify NT and c-Fos mRNA expression. While all antipsychotics increased sNA NT gene expression, only typical drugs affect NT gene transcription in DLST neurons. This difference was also noted when c-Fos mRNA expression was studied in the DLST of the same animals. Interestingly, the increase in sNA NT mRNA was not accompanied by a change in c-Fos message.

We have also studied the effects of chronic (4 week) treatment with haloperidol and with clozapine. We find that the DLST response to haloperidol is reduced over this time period, but not that of the sNA neurons. As with acute treatment, clozapine failed to alter DLST NT mRNA, but as with haloperidol it also caused a sustained elevation of sNA NT message expression. Taken together, these data suggest that the regional specificity of these responses may be related to the motor (DLST) and antipsychotic (sNA) effects of this class of drugs.